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Research Article

Organocatalytic Construction of dihydrocarbazoles via a formal [4+2] Annulation of 3-(indol-3-yl)propanal with 2-chloroacetophenone

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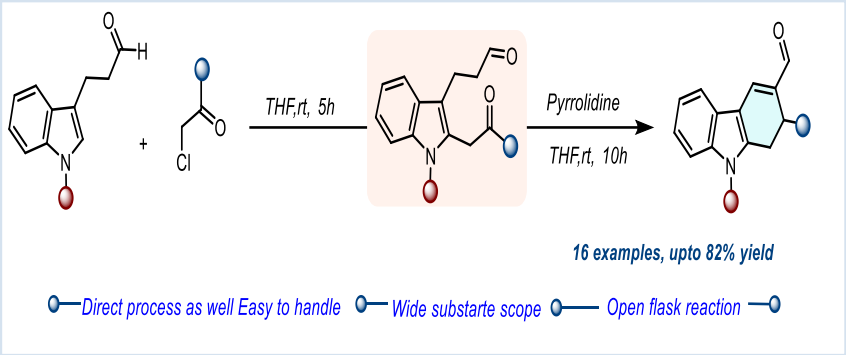
ABSTRACT

A practical one-pot synthetic methodology for the construction of dihydrocarbazole scaffolds has been developed. The sequence proceeds via tandem Friedel-Crafts acylation of followed by pyrrolidine-promoted intramolecular aldol cyclization. This operationally simple protocol delivers fused dihydrocarbazole architectures in a single reaction vessel under mild conditions. The method features broad substrate scope, excellent functional-group tolerance, and provides rapid, scalable access to biologically relevant dihydrocarbazole frameworks via a formal [4+2] annulation strategy.3-(indol-3-yl)propanal derivatives with α-chloroacetophenone.



Scheme1. Organocatalytic Construction of Dihydrocarbazoles.

Introduction

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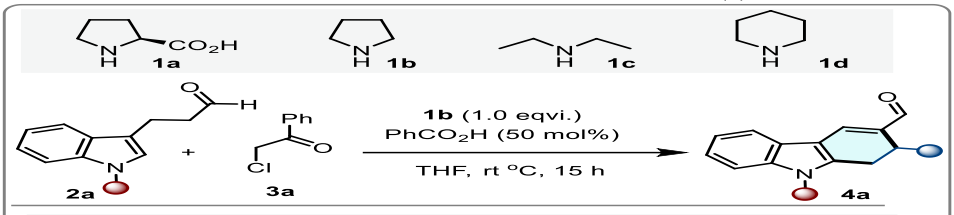
Many natural products and physiologically active substances contain polycyclic carbazole units, especially tetrahydro- and dihydrocarbazoles.1 As a result, numerous efforts have been dedicated to developing efficient methods to construct these privileged structures.2-4 To the best of our knowledge, the catalytic Diels-Alder cycloaddition is the fastest and most efficient method for forming a six-membered ring.5 In order to prepare tetrahydrocarbazoles and dihydrocarbazoles, a variety of substrates, including 2-vinylindoles, 3-vinylindoles6, and o-quinodimethanes (oQDMs)7, have recently been developed as the diene component to react with dienophiles. Carbazole skeletons are present in biologically active compounds. Due to their high activity, stability, and lack of suitable systems, oQDMs have been used in enantioselective Diels-Alder reactions with various complex polycyclic aromatic compounds, though few precedents have been reported.8 pioneering work on using indole-oQDMs in secondary amine-catalyzed asymmetric Diels-Alder reactions by the groups of Melchiorre 9 and Chen,10, the indole-2,3-quinodimethanes have successfully served as active intermediates to construct chiral tetrahydrocarbazoles. in comparison to tetrahydrocarbazoles. The synthesis of dihydrocarbazoles, especially in this way, has received less attention. In 2015, Zanardi et al. reported an elegant method to build linear and angular polycycles embedding a cyclohexadiene carbaldehyde frame via a [4+2] eliminative cycloaddition of extended monocyclic and polycyclic allylidene malononitriles with enals.11 In 2016, Deng and his group reported that 2-methyl-3-carbaldehyde malononitriles could be used as precursors of oQDMs to react with enals to enantioselectively construct dihydrocarbazoles.12

Although these strategies are good for constructing dihydrocarbazoles. But synthesis of dihydrocarbazoles from simple starting materials in one pot remains unmapped, to the best of our knowledge. Thus, developing a direct method for constructing dihydrocarbazoles remains a fascinating challenge. Herein, we present a chronological multicomponent one-pot domino sequence for the first direct construction of dihydrocarbazoles (Scheme 1).

Table 1. Optimization of reaction conditions. [a]



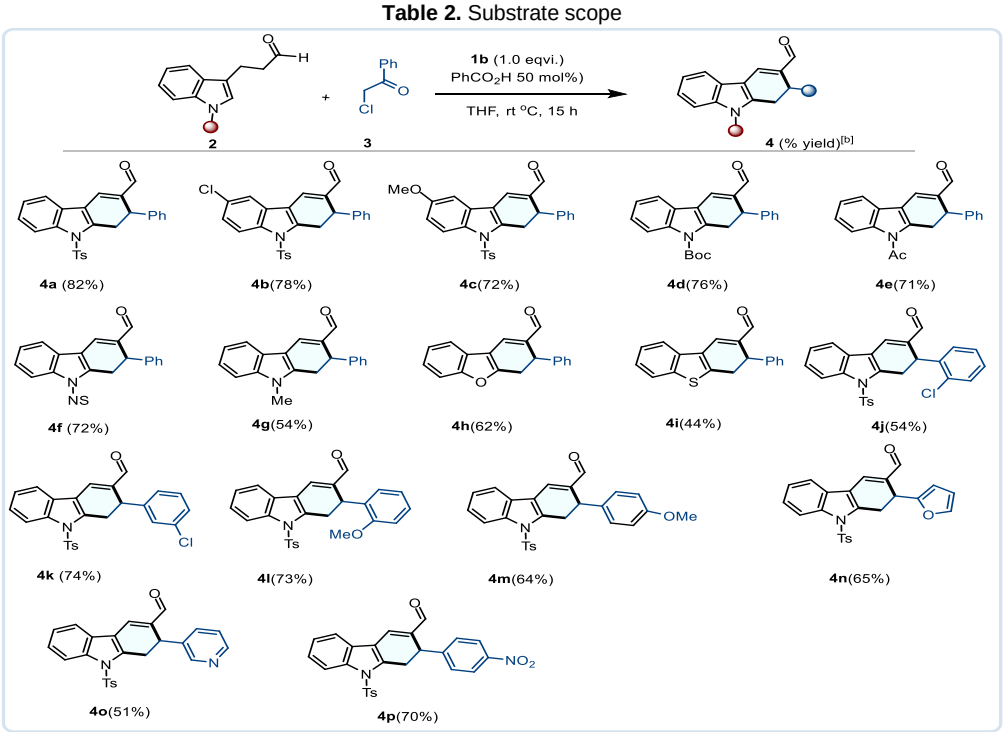
entry	variation from standard conditions	yield (%)[b]
1	**none**	**82**
2	cat. **1a** instead of **1b**	52
3	cat. **1c** instead of **1b**	61
4	cat. **1d** instead of **1b**	39
5	without $PhCO_2H$	20
6	with (30 mol%)$PhCO_2H$	40
7	with (1.0 eqvi.) $PhCO_2H$	82.
8	EtOAc as a solvent	39
9	DMSO as a solvent	<10
10	DMF as a solvent	<10
11	$CHCl_3$ as a solvent	42
12	Toluene as a solvent	32
13	DCM as solvent	44
14	0 °C, 48 h	48

[a] All the reaction was carried out with **2a** (0.3 mmol, 1.0 equiv), **3a** (0.6 mmol, 2.0 equiv), THF (3.0 mL), pyrrolidine **1b** (30 mol%), $PhCO_2H$ (30 mol%), rt 15 h. [b] Isolated yields of **4a** refer to **2a**.

2. Results and discussion

Having an understanding of the reactivity of 3-(indol-3-yl)propanal, we investigated the reaction using 3-(indol-3-yl)propanal **2a** and α-chloroacetophenone **3a** as starting materials, with several amine catalysts, co-catalysts, additives, and solvents to determine the optimized conditions (Table 1). To our delight, under optimized conditions using pyrrolidine ($PhCO_2H$) in THF at rt, [4+2] annulated product **4a** (82% yield) was obtained (entry 1, Table 1). Further variations in terms of amine catalysts, such as proline **1a**, diethylamine **1c,** and piperidine **1d**, did not improve the reaction outcome (entries 2-4, Table 1). The presence of $PhCO_2H$ as a co-catalyst was crucial for the reaction, yielding poor outcomes in its absence (entries 5-7, Table 1). Further screening of different solvents, such as EtOAc, DMSO, DMF, $CHCl_3$, CH_2Cl_2, and toluene (entries 8-13, Table 1), also did not improve the reaction yields. A trace amount of product was observed when the reaction was carried out at 0 °C (entry 14, Table 1), With the standard conditions identified, the generality of the [4+2] annulation reaction was next investigated using **2a** with various **3a** (Table 2). The electronic effect of different substituents on 3-(indol-3-yl)propanal (N-Ts, N-boc, N-Ac, N-NS, N-Me **(4a-4g)** (82 -54 % yield). Moderate yield with 3-(benzofuran-3-yl)propanal and 3-(benzo[b]thiophen-3-yl)propanal **(4h-4i).** whereas Cl and OCH_3 at the different positions of the phenyl ring of α-chloroacetophenone **3j-3m** did not impact the reaction outcome and smoothly led to the formation of the corresponding products **4j-4m** (74–64% yields). To our delight, heteroaromatic-derived α-chloroacetophenones **3n** and **3o** also furnished the corresponding products **4n** and **4o** with good yields. Moreover, α-chloroacetophenone with strong electron-withdrawing groups, such as -NO2 on the aryl ring, produces the expected **4p** products.

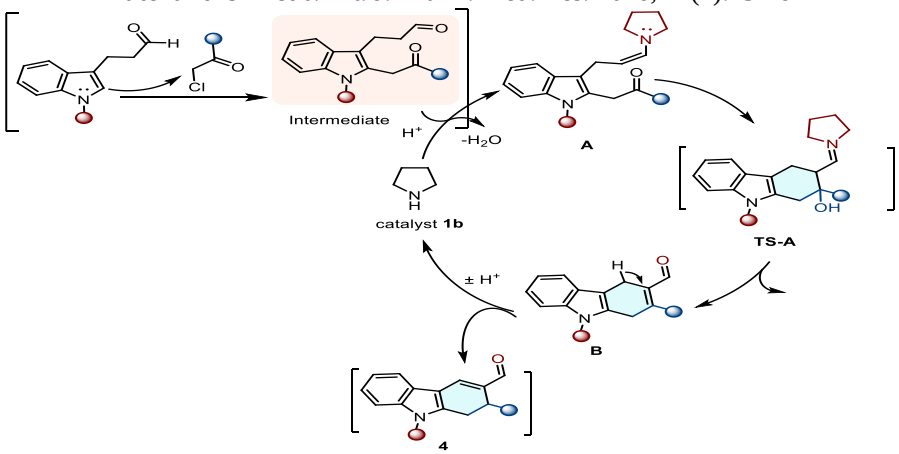
Table 2. Substrate scope



[a] All the reaction was carried out with **2a** (0.3 mmol, 1.0 equiv), and **3a** (0.6 mmol, 2.0 equiv), THF (3.0 mL), pyrrolidine **1b** (30 mol%), $PhCO_2H$ (30 mol%), rt 15 h. [b] Isolated yields of **4a** refer to **2a**.

3. Plausible Mechanism

A plausible mechanism has been proposed based on previous studies in this area and the observed reaction outcomes (Scheme 2). The reaction proceeds through a tandem Friedel-Crafts acylation of 3-(indol-3-yl)propanal derivatives with α-chloroacetophenone, generating a key keto-aldehyde intermediate. Subsequent enamine formation with pyrrolidine **(1b)** triggers an intramolecular aldol-type cyclization via transition state **TS-A**, followed by dehydration and proton transfer to afford the fused dihydrocarbazole product **4.**



Scheme 2. Plausible reaction mechanism for the developed protocol.

4. Materials and Methods.

All commercially available compounds were used as received without further purification. All solvents employed in the reactions were distilled from appropriate drying agents. All reactions under standard conditions were monitored by thin-layer chromatography (TLC) on Merck silica gel 60 F254 precoated plates (0.25 mm). Column chromatographic purification was performed using silica gel (100−200 mesh) and a petroleum ether/EtOAc mixture. Chemical yields refer to pure, isolated substances. ^{1}H, and ^{13}C spectra were recorded in $CDCl_3$/DMSO-d_6 on a BRUKER-AV400 and spectral data were reported in ppm. Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on a Bruker Avance 400 (100 MHz) spectrometer with complete proton decoupling. High-resolution mass spectra were recorded by quadrupole electrospray ionization (ESI). Melting points were determined by an EZ-Melt, Automated Melting Point Apparatus.

5.0. Typical procedure for [4+2] annulation to access dihydrocarbazole

A 20 mL oven-dried Schlenk reaction tube was charged with .3-(indol-3-yl)propanal **2a** (0.3 mmol, 1 equiv.), α-chloroacetophenone **3a** (0.6 mmol, 2.0 equiv.), pyrrolidine (6 mg, 0.09 mmol, 30 mol%), $PhCO_2H$ (11 mg, 0.09 mmol, 30 mol%) in THF (5.0 mL) under rt for 15 h. The progress of the reaction was monitored by TLC; after completion, the reaction mixture was cooled to rt and stirred between aqueous $NaHCO_3$ (3.0 mL) and EtOAc (3.0 mL). The organic layer was separated, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo; the crude products were purified by column chromatography using petroleum ether/EtOAc as the eluent, yielding **4a**.

Compound 4a: 69 mg, yield 82%, light yellow solid, m.p : 195-198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.66 (s, 1H), 8.13 (dd, 6.1, 3.3 Hz, 1H), 7.68 (s, 1H), 7.64 (dd, J= 6.0, 3.1 Hz, 1H), 7.33 (td, J=6.4, 2.6 Hz, 4H), 7.21-7.09 (m, 5H), 6.97 (d, J= 8.0 Hz, 2H), 4.47 (d, J= 9.3 Hz, 1H), 3.99 (d, J= 18.7 Hz, 1H), 3.60 (dd, J= 18.7, 9.4 Hz,1H), 2.28 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.3,145.3,141.4,139.2, 138.1, 137.1, 137.0, 135.0,130.1,128.8,127.0,127.0,126.7,126.6,125.1, 124.4,118.1,116.8,114.8, 36.0, 31.8, 21.7. **HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C26H22NO3S: 428.1242, found: 427.1244.

Compound 4b: 66 mg, yield 78%; yellow solid, m.p: 188-191 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.65 (s, 1H), 8.05 (d, J = 8.9 Hz,1H), 7.61 (s, 2H), 7.49-7.42 (m,1H), 7.29 (d, J = 8.2 Hz, 2H), 7.18-7.08 (m, 5H), 6.97 (d, J = 8.2 Hz, 2H), 4.46 (d, J = 9.1 Hz,1H), 3.96 (d, J = 18.7 Hz, 1H), 3.58 (dd, J = 18.8, 9.5 Hz, 1H), 2.30 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 2,157.1, 145.0, 141.3, 139.7, 138.0,136.6, 134.9, 131.4, 129.9, 128.7, 127.6, 126.9, 126.9, 126.4, 116.7, 115.6, 113.4, 100.7, 55.7, 35.9, 31.7, 21.6; **HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C26H21ClNO3S: 462.0823, found: 462.0831.

Compound 4c : 61 mg, yield 72%; yellow solid, m.p: 181-183 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.65 (s, 1H), 8.01 (d, J = 9.1 Hz, 1H), 7.65 (s, 1H), 7.30 (d, J = 8.3 Hz, 2H), 7.17 (dd, J = 7.9, 5.1 Hz,1H), 7.15e7.11 (m, 3H), 7.07 (d, J = 2.4 Hz,1H), 6.94 (dd, J = 11.7, 7.5 Hz, 3H), 4.45 (d, J = 8.8 Hz, 1H), 3.96 (d, J = 18.8 Hz, 1H), 3.87 (s, 3H), 3.57 (dd, J = 18.8, 9.4 Hz, 1H), 2.28 (s, 3H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.2, 157.2, 145.0, 141.3, 139.7, 138.0, 136.7, 134.9, 131.4 129.9, 128.7, 127.6, 126.9, 126.9, 126.4, 116.7, 115.6,113.4,100.7, 55.7, 35.9, 31.7, 21.6; **HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C27H24NO4S: 458.1348, found: 457, 1347

Compound 4d: 64 mg, yield 76%; light yellow oil; **^{1}H NMR (400 MHz, $CDCl_3$)** δ. 64(s,1H), 8.16e8.09(m,1H),7.67 (d, J = 8.2 Hz, 2H), 7.35-7.31 (m, 2H), 7.24 (d, J = 7.1 Hz, 2H), 7.20e7.15 (m, 3H), 4.44 (d, J = 9.7 Hz, 1H), 3.90 (d, J = 19.2 Hz, 1H), 3.60 (dd, J = 19.2, 10.0 Hz,1H),1.66 (s **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.3,149.7, 143.0, 140.5, 138.5, 136.9, 136.0, 128.6, 126.9, 126.9, 126.3, 124.5, 123.7, 117.5, 115.9, 115.3, 85.3, 35.8, 31.7, 29.7, 28. **HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C24H24NO3 : 374.1678, found: 374.1679.

Compound 4e: 61mg, yield 71%; yellow solid, m.p: 131-133 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.66(s,1H), 8.05-7.93 (m, 1H), 7.71 (d, J = 7.3 Hz, 2H), 7.42e7.34 (m, 3H), 7.18 (dt, J¼12.1, 6.1 Hz, 5H), 4.45 (d, J = 8.8 Hz,1H), 3.80 (d, J = 17.7 Hz,1H), 3.68 (dd, J = 18.9, 9.7 Hz, 1H), 2.73 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.2, 169.8, 142.5,139.7,137.8,136.7, 136.5,128.7,127.0,126.9,126.8,124.9,124.1, 117.9, 116.2,115.4, 36.1, 32.4, 27.5**HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C21H18NO2: 316.1259, found: 316.1260.

Compound 4f: 61 mg, yield 72%; yellow solid, m.p: 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.70(s,1H), 8.14-8.10(m, 1H), 7.91 (d, J = 8.9 Hz, 2H), 7.72 (s, 1H), 7.71 = 7.66 (m, 1H), 7.47 (d, J = 8.9 Hz, 2H), 7.41-7.38 (m, 3H), 7.21 (d, J = 7.2 Hz, 1H), 7.14 (t, J = 7.5 Hz, 2H), 7.09 (d, J = 7.3 Hz, 2H), 4.50 (d, J = 8.9 Hz,1H), 3.89 (d, J = 18.7 Hz, 1H), 3.62 (dd, J = 18.7, 9.2 Hz, 1H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.0, 150.3, 142.9, 140.4, 138.0, 137.4, 137.3, 136.9, 128.9, 127.5, 127.2, 126.9, 126.7, 125.6,125.0,124.5,118.4, 118.1, 114.6, 35.9, 32.3; **HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C25H19N2O5S: 459.0936, found: 459.0935.

Compound 4g : 45 mg, yield 54%; yellow solid, mp: 123-1- 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.67 (s, 1H), 8.09 (d, J = 7.1 Hz,1H), 7.79 (s,1H), 7.65 (d, J = 8.4 Hz,1H), 7.36-7.31 (m, 2H), 7.18 (dd, J = 15.3, 8.2 Hz, 3H), 6.91 (dd, J = 12.4, 8.2 Hz, 3H), 6.71 (d, J = 7.5 Hz, 1H), 6.57 (t, J = 7.5 Hz, 1H), 4.90 (d, J = 9.2 Hz, 1H), 3.93 (s, 3H), 3.93 (d, J = 9.2 Hz,1H), 3.47 (dd, J = 18.9, 9.6 Hz,1H), 2.25 (s, 3H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.2,156.7, 144.8, 140.1, 138.9, 136.9, 136.6, 134.8, 129.8, 127.9, 127.6, 126.8, 126.6, 126.2, 124.7, 124.2, 120.1,117.8,116.4,114.7,110.9, 55.6, 30.0, 29.3, 21.5; **HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C27H24NO4S: 458.1348, found: 458.1347

Compound 4h: 33 mg, yield 62%; orange solid, m.p: 170-173 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.64(s,1H),7.67e-.62 (m, 2H), 7.51 7.46 (m,1H), 7.33 (t, J = 6.8 Hz, 2H), 7.16 (m, 5H),4.50 (d, J = 10.0 Hz,1H), 3.59 (dd, J = 18.5, 10.3 Hz,1H), 3.26 (d, J = 19.0 Hz, 1H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.1, 159.6, 155.8, 142.2, 138.4, 136.6, 128.7, 127.2, 126.8, 124.7, 124.4, 123.8, 118.5, 113.2,111.8, 36.3, 30.2. **HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C19H15O2: 275.0994, found: 275.0993.

Compound 4i: 25 mg, yield 44%; orange solid, m.p: 161-164 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.70 (s, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.69 (s, 1H), 7.47 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 7.4 Hz,1H), 7.22-7.12 (m, 5H), 4.42 (d, J = 9.0 Hz,1H), 3.60 (dd, J = 17.7, 9.4 Hz, 1H), 3.36 (d, J¼ =.7 Hz, 1H **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.9, 144.7, 142.0, 139.1, 138.2, 137.4, 136.2, 128.6, 127.9, 127.0, 127.0, 125.2, 124.7, 122.8, 120.2, 35.8, 31.9**HRMS (ESI-TOF)** *m/z*: [M + H$^+$] Calcd for C19H15OS: 291.0765, found: 291.0767.

Compound 4j: 48 mg, yield 54%; yellow solid, mp: 212-215 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.66(s,1H),8.19-8.12 (m, 1H), 7.82 (s,1H), 7.70-7.64 (m,1H), 7.42 (d, J = 7.9 Hz,1H), 7.40-.33 (m, 2H), 7.30 (d, J = 8.3 Hz, 2H), 7.11 (t, J = 7.6 Hz, 1H), 6.91 (d, J =8.1 Hz, 2H), 6.83 (t, J = 7.5 Hz, 1H), 6.76 (d, J = 7.7 Hz, 1H), 4.89 (d, J =9.5 Hz, 1H), 3.91 (d, J = 18.9 Hz,1H), 3.54 (dd, J = 18.9, 9.8 Hz,1H), 2.25 (s, 3H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 190.7,145.0,139.1,138.9, 137.1, 137.0, 135.9, 134.9, 133.4, 130.3, 129.9, 128.0, 127.5, 126.6,

126.3,126.1,125.0,124.3,117.9,116.3,114.7, 32.6, 29.6, 21.5. **HRMS (ESI-TOF)** *m/z*: [M + H^+] Calcd for C26H22ClNO3S: 462.0823, found: 462.0831

Compound 4k: 65 mg, yield 74 %; yellow solid, m.p: 153-156 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.65(s,1H),8.21e-.15 (m, 1H), 7.70 (s, 1H), 7.68- 7.63 (m, 1H), 7.36 (d, J = 7.2 Hz, 4H), 7.14 (d, J = 7.7 Hz, 1H), 7.07 (t, J = 7.9 Hz, 1H), 7.04- 6.97 (m, 4H), 4.41 (d, J = 9.4 Hz, 1H), 3.89 (d, J¼ = 8.8 Hz,1H), 3.59 (dd, J = 18.9, 9.6 Hz,1H), 2.30 (s, 3H) .**^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 190.9,145.4,143.4,138.5, 138.2, 137.1, 136.0, 134.9, 134.3, 130.0, 129.9, 127.1, 126.8, 126.3, 126.2, 125.3, 125.1, 124.4, 118.0, 116.5, 114.7. . **HRMS (ESI-TOF)** *m/z*: [M + H^+] Calcd for C26H22ClNO3S: 462.0823, found: 462.0830.

Compound 4l: 65 mg, yield 73 %; yellow solid, m.p: 123-125 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.67 (s, 1H), 8.09 (d, J = .1 Hz,1H), 7.79 (s,1H), 7.65 (d, J = 8.4 Hz,1H), 7.36 -7.31 (m, 2H), 7.18 (dd, J = 15.3, 8.2 Hz, 3H), 6.91 (dd, J = 12.4, 8.2 Hz, 3H), 6.71 (d, J = 7.5 Hz, 1H), 6.57 (t, J =7.5 Hz, 1H), 4.90 (d, J = 9.2 Hz, 1H), 3.93 (s, 3H), 3.93 (d, J = 9.2 Hz,1H), 3.47 (dd, J = 18.9, 9.6 Hz,1H), 2.25 (s, 3H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.2,156.7, 144.8, 140.1, 138.9, 136.9, 136.6, 134.8, 129.8, 127.9, 127.6, 126.8, 126.6, 126.2, 124.7, 124.2, 120.1,117.8,116.4,114.7,110.9, 55.6, 30.0, 29.3, 21.5. **HRMS (ESI-TOF)** *m/z*: [M + H^+] Calcd for C27H24NO4S: 458.1348, found: 458.1347.

Compound 4m: 57 mg, yield 64%; yellow solid, m.p: 138-140 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.65(s,1H), 8.26-8.10(m, 1H), 7.64 (d, J = 6.6 Hz, 2H), 7.34 (d, J = 8.7 Hz, 4H), 7.00 (dd, J = 18.4, 8.4 Hz, 4H), 6.65 (d, J = 8.6 Hz, 2H), 4.41 (d, J = 9.0 Hz, 1H), 3.95 (d, J =18.7 Hz, 1H), 3.74 (s, 3H), 3.55 (dd, J = 18.6, 9.3 Hz, 1H), 2.29 (s, 3H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 191.2, 158.5, 145.1, 139.0, 137.7, 137.2, 136.9, 135.0, 133.3, 129.9, 127.9, 126.5, 126.4, 124.9, 124.2, 117.9, 116.6, 114.7, 113.9, 55.1, 35.1, 31.8, 21.5. **HRMS (ESI-TOF)** *m/z*: [M + H^+] Calcd for C27H24NO4S : 458.1348, found: 458.1351.

Compound 4n: 56 mg, yield 66%; brown solid, m.p: 124-127 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ d 9.69 (s, 1H), 8.13 (d, J = 8.7 Hz,1H), 7.62 (s,1H), 7.57 (d, J = 8.1 Hz, 2H), 7.37 -7.29 (m, 3H), 7.21 (d, J = 5.1 Hz,1H), 7.15 (d, J = 8.2 Hz, 2H), 6.12 (s,1H), 5.82 (s,1H), 4.57 (d, J = 8.3 Hz, 1H), 4.24 (d, J = 18.6 Hz, 1H), 3.36 (dd, J = 18.8, 8.6 Hz, 2H), 2.33 (s, 3H) .**^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 190.8,148.6, 148.2, 145.5, 138.3, 138.2, 137.1, 136.8, 135.7, 135.0, 134.5, 130.0, 126.2, 126.2, 125.3, 124.4, 123.4, 33.7, 31.1, 21.6; . **HRMS (ESI-TOF)** *m/z*: [M + H^+] Calcd for C24H20NO4S: 418.1035, found: 418.1036.

Compound 4o: 43mg, yield 5%; yellow solid, mp: 151-153 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.65 (s,1H), 8.42 (s,1H), 8.18 (d, J = 9.0 Hz,1H), 7.71 (s,1H), 7.71-7.60 (m,1H), 7.44-7.33 (m, 5H), 7.08-6.95 (m, 3H), 4.45 (d, J = 9.2 Hz, 1H), 3.89 (d, J =18.7 Hz, 1H), 3.61 (dd, J =18.8, 9.4 Hz, 1H), 2.31 (s, 3H); **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 190.8, 148.6, 148.2, 145.5, 138.3, 138.2, 137.1, 136.76, 135.7, 135.0, 134.5, 130.0, 126.2, 126.2, 125.3, 124.4, 123.4, 33.7, 31.1, 21.6. **HRMS (ESI-TOF)** *m/z*: [M + H^+] Calcd for C25H21N2O3S: 429.1195, found: 429.1194.

Compound 4p: 60 mg, yield 70%; yellow solid, m.p: 198 °C).**^{1}H NMR (400 MHz, $CDCl_3$)** δ 9.65 (s, 1H), 8.22 (d, J = 8.8 Hz, 1H), 7.94 (d, J = 8.7 Hz, 2H), 7.73 (s, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.41 (t, J = 7.0 Hz, 4H), 7.24 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 8.1 Hz, 2H), 4.52 (d, J = 9.1 Hz,1H), 3.87 (d, J = 18.7 Hz,1H), 3.63 (dd, J = 18.9, 9.6 Hz, 1H), 2.28 (s, 3H). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$)** δ 190.8, 149.0, 146.9, 145.9, 138.5, 138.1, 137.2, 135.6, 135.2, 130.0, 127.8, 126.2, 126.11, 125.4, 124.6, 123.8, 118.0, 116.5, 114.8, 35.8, 30.9, 21.4. **HRMS (ESI-TOF)** *m/z*: [M + H^+] Calcd for C26H21N2O5S: 473.1093, found: 473.1094.

Conclusion

In summary, we have developed a practical and operationally simple one-pot synthetic protocol for the direct construction of dihydrocarbazole scaffolds from readily accessible 3-(indol-3-yl)propanal derivatives and α-chloroacetophenones. The methodology exploits a tandem sequence involving Friedel-Crafts acylation followed by pyrrolidine-promoted intramolecular aldol cyclization, enabling rapid assembly of fused carbazole architectures in a single reaction vessel under mild conditions. This formal [4+2] annulation strategy provides an organocatalytic alternative to metal-dependent approaches for accessing biologically relevant dihydrocarbazole frameworks, featuring broad substrate scope and excellent functional-group tolerance. Given the prevalence of carbazole motifs in natural products and pharmaceutically active compounds.

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